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09/594,983	06/15/2000	William C. Olson	57906-B/JPW/SHS	8686

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EXAMINER	
FOLEY, SHANON A	
ART UNIT	PAPER NUMBER
1648	10

DATE MAILED: 03/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/594,983	Applicant(s) WILLIAM C. OLSEN ET AL.	
	Examin r Shanon A. Foley	Art Unit 1648	

-- Th MAILING DATE of this communication appears on the cover sh et with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *78-99* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *78-98* is/are rejected.

7)☒ Claim(s) *98 and 99* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 June 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5+2'ls
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Error Report* + Notice to Comply

DETAILED ACTION

The Examiner of your application has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1648, Examiner Foley.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Election/Restrictions

Applicant's election of group V and species PA14 with traverse is acknowledged. Restriction between the humanized and non-humanized monoclonal antibody forms is withdrawn. Therefore, all pending claims 78-99 are under consideration. Should the elected species PA14 be free of prior art, a subsequent search for the other species will ensue.

Specification

The abstract of the disclosure is objected to because it must be 150 words or less. Correction is required. See MPEP § 602 (j).

Drawings

The drawing of Figure 4 is objected to because the numbers in the boxes are very hard to read. A proposed drawing correction or corrected drawings are required in reply to the Office

action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Objections

Claims 88, 89, and 98 are objected to because of the following informalities: "P11" is presumably "PA11". Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 78-88 and 90-98 are provisionally rejected under the judicially created doctrine of double patenting over claims 78 and 79, 80, respectively, of copending Application No. 09/464,9052. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: monoclonal antibody PA14 and any other antibody that binds to the same epitope as PA14.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 93 and 95-97 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 93 is vague and indefinite because the metes and bounds of what is intended or encompassed by "some, most, or all of the amino acids" in lines 1-2 and 4-5 cannot be determined.

Claims 95 and 96 state that donor immunoglobulin comprises "the CDRs". Which CDRs are being referred to?

Claims 96 and 97 are confusing because claim 96 states that the framework of a donor immunoglobulin is derived from a human immunoglobulin, while the donor immunoglobulin is murine in claim 97. Is the framework of the antibody derived from human, except for the murine amino acids immediately adjacent to the CDRs? Or, can there be two possible donors for each humanized antibody, i.e., one from human and another from murine?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 88, 89 and 98 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that hybridomas to make monoclonal antibodies PA8-PA12 and PA14 are required to practice the claimed invention because they are necessary limitations for the success of the invention as stated in the claims. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the hybridomas that make monoclonal antibodies PA8-PA12 and PA14. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining the hybridomas that make monoclonal antibodies PA8-PA12 and PA14 and it is not apparent if it is readily to the public. Applicant's deposit statement on specification pages 13-14 does not indicate the extent of public availability. If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 78-88, 90, 91, 93, 94, and 97 are rejected under 35 U.S.C. 102(a) as being anticipated by Wu et al. (WO 98/18826).

The claims are drawn to a monoclonal antibody that binds to the N-terminus and/or one of three extracellular loops of CCR5 and is humanized by incorporation of a human immunoglobulin framework.

Wu et al. teaches that monoclonal antibodies 5C7 and 3A9 are both specific for the N-terminus of the CCR5 receptor and monoclonal antibody 2D7, which was generated from murine IgG1, has epitope specificity for the second extracellular loop of the CCR5 receptor, see page 15, lines 18-21 and page 72, line 31, and claims 1-3, 27-29, 55, and 56. Wu et al. also teaches a bispecific antibody that binds to the N-terminus and the second extracellular loop of CCR5, see page 15, line 27 to page 16, line 5, and humanized forms of the antibodies, where the framework and the consensus are derived from a human immunoglobulin or multiple immunoglobulin molecules, where the regions surrounding the CDR regions have been replaced by human immunoglobulin molecules, see page 19, line 31 to page 21, line 32. Claims 80 and 82-87 are drawn to the epitope comprising specific amino acid sequences. Although Wu et al. do not specifically teach the amino acid sequences within the epitopes at the N–terminus and the second

extracellular loop, it is known in the art that the specific amino acids in claims 80, 82-87 exist in these CCR5 regions, evidenced by Chen et al. (Journal of Virology. 1997; 71 (4): 2705-2714, see especially page 2708). Therefore, the monoclonal antibodies 5C7, 3A9, and 2D7 of Wu et al. bind to CCR5 epitopes that inherently possess the claimed amino acids.

Claims 78-83 and 88 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Wu et al. (J. Exper. Med. Oct. 1997; 186 (8): 1373-1381).

The claims are drawn to a monoclonal antibody that binds to the N-terminus or one of the three extracellular loops of CCR5.

Wu et al. teaches a monoclonal antibody, murine IgG1 2D7, which binds to the second extracellular loop of CCR5 and another monoclonal antibody, 3A9, which binds to the N-terminal region of CCR5, see the second paragraph of the second column on page 1374 and the paragraph bridging the columns on page 1375. Although Wu et al. do not specifically teach the amino acid sequences within the epitopes at the N–terminus and the second extracellular loop, it is known in the art that the specific amino acids in claims 80, 82-83 exist in these CCR5 regions, evidenced by Chen et al. (Journal of Virology. 1997; 71 (4): 2705-2714, see especially page 2708). Therefore, the monoclonal antibodies 3A9 and 2D7 of Wu et al. bind to CCR5 epitopes that inherently possess the claimed amino acids.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 84-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al. (J. Exper. Med. Oct. 1997; 186 (8): 1373-1381) and in further view of Hill et al. (Virology. Sept. 1998; 248: 357-371).

The claims are drawn to a monoclonal antibody to CCR5 that binds to an epitope at the N-terminus and the second extracellular loop of CCR5.

See the teachings of Wu et al. above. Wu et al. does not teach a monoclonal antibody with specificity to an epitope on both the N-terminus and the second extracellular loop of CCR5, but does teach monoclonal antibodies that separately bind to each of these regions.

One of ordinary skill in the art at the time the invention was made would have been motivated to make a bispecific antibody that binds to the N-terminus and the second extracellular loop of CCR5 to effectively inhibit HIV virus entry and inhibit any HIV virus that binds to either or both epitopes. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation in producing the claimed invention because Hill et al. teaches that the N-terminus of CCR5 plays an essential role in the entry of diverse HIV envelope proteins. Wu et al. teaches that the second extracellular loop of CCR5 is an ideal target site for HIV inhibitors and that efficient inhibition of HIV is achieved by monoclonal antibody recognition of either the second extracellular loop or the N-terminus of CCR5. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 90-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al. (J. Exper. Med. Oct. 1997; 186 (8): 1373-1381).

The claims are drawn to a humanized form of the instant monoclonal antibody that binds to the N-terminus or the second extracellular loop of CCR5 and product-by-process construction of the humanized antibody.

See the teachings of Wu et al. above. Wu et al. does not teach a humanized form of the monoclonal antibody 2D7 or 3A9.

However, one of ordinary skill in the art at the time the invention was made would have been motivated to humanize the monoclonal antibody of Wu et al. to characterize host immune response and antibody efficiency and effectiveness for use in *in vivo* assays. A humanized form of the monoclonal antibody of Wu et al. would have the added advantage eliciting a diminished immune response against the recombinant antibody, while retaining the desired functional capacity of reacting with the specific epitope. Further, one of ordinary skill in the art would have been motivated to use the human immunoglobulin framework to maintain the conformation of the CDR region from the no-humanized form. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation in producing a humanized antibody of Wu et al. because conventional techniques for humanizing antibodies are known in the art. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 92, 95, and 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al. WO 98/18826 or in the alternative, Wu et al. (J. Exper. Med. Oct. 1997; 186 (8): 1373-1381).

The claims are drawn to the monoclonal antibody containing a framework from a human immunoglobulin IgG1, IgG2, IgG3, IgG4, IgA, or IgM.

See the teachings of Wu et al. above (both references). Neither reference teaches the framework of the monoclonal antibodies to be IgG1, IgG2, IgG3, IgG4, IgA, or IgM. However, it would have been obvious for one of ordinary skill in the art at the time the invention was made to obtain the antibody framework from any of the human immunoglobulins to maintain the conformation of the CDR region and to render the recombinant antibodies less immunogenic once administered. Further, one of ordinary skill in the art would have been motivated to maintain the donor amino acid sequences immediately adjacent to the CDR domains to assure that when the framework portion of the antibody is added, the CDR domain remains intact. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the claimed invention because humanizing antibodies using human IgG is conventional technique for humanizing recombinant antibodies. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Allowable Subject Matter

Claims 98 and 99 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and satisfaction of all deposit and availability requirements under the Budapest Treaty.

Claims 98 and 99 are drawn to allowable subject matter because the prior art does not teach or suggest the instant monoclonal antibodies or the hybridomas producing the antibodies. These claims would be allowable if claim 98 were drafted in independent form

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon A. Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SAF
Shanon Foley/SAF
February 27, 2002

James C. Housel 3/11/02

JAMES HOUSEL
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